COPY

REQUEST FOR TRADEMARK REVIEW

TO: Labeling and Nomenclature Committee
Attention: Dan Boring, Chair, (HFD-530) CRP2

FROM: Division of Anti-inflammatory, Analgesic and Ophthalmic Products, HFD-550
Attention: Charlotte Yaciw Phone: 827-2511

HFD 10-3-96

DATE: October 2, 1996

SUBJECT: Request for Assessment of a Trademark for a Proposed Drug Product

NDA Number: 20-612

Proposed Trademark: Lidoderm Patch

Company Name: Hind Health Care

Established name, including dosage form: lidocaine transdermal patch

Other trademarks by the same firm for companion products: none

Indications for Use (may be a summary if proposed statement is lengthy): Treatment of chronic pain in post-herpetic neuralgia (intensely painful skin subsequent to an outbreak of shingles)

Initial comments from the submitter (concerns, observations, etc.): This is an orphan drug. Precedent is the Nicoderm (nicotine) patch

Note: Meetings of the Committee are scheduled for the 4th Tuesday of the month. Please submit this form at least one week ahead of the meeting. Responses will be as timely as possible.

Rev Oct 96

Consult #689 (HFD-530)

LIDODERM PATCH lidocaine transdermal patch

There were no look-alike/sound-alike conflicts or misleading aspects noted with the proposed proprietary name. However, the Committee believes the established name for the product is (lidocaine transdermal system). The USP does not specifically recognize the term "patch" and to be in conformance with the USP established name conventions, "patch" should not be used.

The Committee has no reason to find the proposed proprietary name unacceptable.

D Boring 11/18/96, Chair
CDER Labeling and Nomenclature Committee

May 30, 1996

Preapproval Certification

LIDOCAINE PATCH

NDA 20-612

This is to certify that Hind Health Care, Inc. has provided under Good Manufacturing Practices, a true and complete copy of the Chemistry, Manufacturing and Control Section and application form.

Furthermore, Hind Health Care certifies that the manufacturer of Lidocaine Patch (NDA 20-612) manufactures and packages product in conformance with Good Manufacturing Practices (GMP).

Signed:

Harry W Hind
Harry W. Hind
President, Hind Health Care, Inc.

5-31-96
Date

Mutagenesis:
Lidocaine HCl is not mutagenic in Salmonell/mammalian microsome test nor clastogenic in chromosmome aberration assay with human lymphocytes and mouse micronucleus test.

March 18, 1999

NDA 20-612
DRUG: LIDODERM PATCH (lidocaine gel)
SPONSOR: HIND HEALTH CARE
45-DAY FILING MEETING MINUTES

PRESENT: W. Chambers, H. Patel, R. Neuner, R. Stein, J. Yang, C. Yaciw, C. Koerner

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CHEMISTRY:

Drug Substance: The sponsor has switched drug substance vendor. Upon superficial review of the DMF from new vendor [redacted] and old vendor [redacted] they appear similar.

Drug Product: The sponsor will need to commit to making another batch of Drug product using a third batch of drug substance. Zero - time point stability data will need to be submitted. The sponsor has submitted 0 time point stability data for three batches of drug product using two batches of drug substance.

The sponsor will need to commit to providing full release data on newly made validation batches as they did with the drug product used in the clinical studies.

Dissolution: The sponsor will need to commit to performing a comparative dissolution study between the newly made drug product
for marketing and the drug product used in the clinical studies.

Packaging: The sponsor will need to conduct compatibility studies of the drug product with proposed packaging.

English Translations: The sponsor will need to complete any remaining Japanese in the application into English.

Stability: the sponsor will need to submit a protocol for post approval stability testing. We will also need a statement of commitment to conduct these studies.

The application is fileable.Projected completion date: mid November 1996

PHARMACOLOGY:
The reviewer requests copies of references cited for the information cited in the proposed labeling, such as mutagenesis and impairment of fertility.

The application is fileable. Projected completion date: mid October, 1996

STATISTICS:
No issues

The application is fileable. Projected completion date: Mid October 1996

CLINICAL:
The medical officer was concerned that the sponsor did not conduct adequate skin safety studies (repeat irritation, photoallergy, vena puncture) in patients of different skin pigmentation (Asians and African-Americans).
It was decided by the Division Director that these studies would be difficult to conduct and will not be asked of the sponsor.

The application is fileable. Projected completion date: mid October, 1996.

Submitted by Koerner
saved as 20612fm6.722

CC:
NDA 20-612
HFD-550 Div Files
HFD- 550 Koerner

NDA 20-612

DATE: JULY 21, 1997

Sponsor

DRUG: LIDODERM PATCH

SPONSOR: HIND HEALTH CARE

SUBJECT: DISCUSSION OF NA LETTER

PRESENT
Sponsor: L. Caldwell, H. Hind, J. Quiring, H. Fields, M. Rowbotham
FDA: M. Weintraub, MJ Walling, H. Hyde, W. Chambers, R. Stein, V. Lutwak, C. Koerner

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Overview:
The sponsor received a Not Approvable letter based on a lack of demonstrated efficacy in the proposed indication of PHN for the product, Lidoderm Patch. Additionally, there were CMC deficiencies. The sponsor has chosen to devote this meeting to discussion of the clinical issues only.

Meeting Minutes:
The Division relayed that an additional efficacy study would be required.

A randomized withdraw study design was recommended. Patients presently doing well on the Patch could be randomized to either placebo or remain on the test product.

The duration of the study should be at least 2-4 weeks in order to assess chronic use efficacy.

The test product would need to perform statistically better than the placebo patch.

The sponsor will submit responses to the CMC deficiencies and their proposed protocol for the confirmatory efficacy study for review.

Submitted by Koerner CK 7/28/97
saved as sm7.721

cc:
NDA 20-612
Div Files
HFD-550 Koerner, Hyde, Weintraub

NDA 20-612

DATE: JULY 9, 1997

DRUG: LIDODERM PATCH

SPONSOR: HIND HEALTH CARE

SUBJECT: DISCUSSION OF NA LETTER

PRESENT: M. Weintraub, J. Hyde, R. Stein, MJ Walling, V. Lutwak

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Overview

This application was Not Approved because of the following:

- The study showed no difference between placebo patches and treatment patches for primary endpoints as specified in the protocol.
- The endpoint which demonstrated efficacy (Allodynia) was not in the original protocol and was a secondary endpoint in the successful study.
- The methods used in measuring allodynia efficacy was of unknown clinical significance.
- A number of chemistry issues.

Meeting Minutes

The sponsor has chosen to dedicate the upcoming July 21, 1997 meeting to clinical issues only.

The Division will recommend another study be conducted. If the result is positive this study could be substantial evidence for an approval of the product for PHN.

Recommendations:

- Sufficient duration of study must be conducted
- Placebo and Lidoderm Patches should be compared
- Randomized withdraw design should be considered
- Appropriate endpoints for PHN must be measured

Submitted by Koerner
saved as 20612Tm7.09

CC:
NDA 20-612
HFD-550 Div Files
HFD- 550 M. Weintraub, J. Hyde, R. Stein, MJ Walling, V. Lutwak

NDA 20-612

DATE: JULY 9, 1997

DRUG: LIDODERM PATCH

SPONSOR: HIND HEALTH CARE

SUBJECT: DISCUSSION PROPOSED CLINICAL PROTOCOL RESPONDING TO THE NA LETTER

PRESENT
FDA: M. Weintraub, H. Hyde, R. Stein, C. Koerner

Comments and questions regarding the proposed clinical protocol of August 30, 1997 as a response to the Not Approvable letter.

What is the definition of "baseline"?

When will the patients be randomized?

How many patients will be in the study?

What is the definition of "exit" from treatment.

The division recommends that an assessment of blinding be conducted at 48 hrs.

Will a 2 tail test or a 1 tail test be conducted for efficacy (page 10)?

What is the sponsor's intent for "drop outs? What is the meaning of "high level"?

The division is willing to review and provide comments on a revised protocol based on today's telecon.

Submitted by Koerner
saved as tm7.010

NDA 20-612

DATE: JULY 9, 1997

DRUG: LIDODERM PATCH

SPONSOR: HIND HEALTH CARE

SUBJECT: DISCUSSION OF NA LETTER

PRESENT
Sponsor: L. Caldwell, H. Hind, J. Quiring, H. Fields, M. Rowbotham
FDA: M. Weintraub, MJ Walling, H. Hyde, W. Chambers, R. Stein, V. Lutwak, C. Koerner

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Overview:
The sponsor received a Not Approvable letter based on a lack of demonstrated efficacy in the proposed indication of PHN for the product, Lidoderm Patch. Additionally, there were CMC deficiencies. The sponsor has chosen to devote this meeting to discussion of the clinical issues only.

Meeting Minutes:
The Division relayed that an additional efficacy study would be required.

A randomized withdraw study design was recommended. Patients presently doing well on the Patch could be randomized to either placebo or remain on the test product.

The duration of the study should be at least 2-4 weeks in order to assess chronic use efficacy.

The test product would need to perform statistically better than the placebo patch.

The sponsor will submit responses to the CMC deficiencies and their proposed protocol for the confirmatory efficacy study for review.

Submitted by Koerner
saved as sm7.721

cc:
NDA 20-612
Div Files
HFD-550 Koerner, Hyde, Weintraub

HFD-550/ Koerner.

RECORD OF TELECON
NDA 20-612
DATE: October 17 and November 18, 1997
DRUG: Lidoderm Patch
SPONSOR: Hind Health Care
SUBJECT: Discussion of proposed clinical protocol responding to the not approvable letter

PRESENT
Sponsor: L. Caldwell
FDA: M. Weintraub, H. Hyde, R. Stein, C. Koerner

OVERVIEW:
The purpose of this telecon is to discuss the clinical protocol submitted by the sponsor in response to the NA letter where lack of efficacy was cited as a major deficiency.

- What is the definition of "baseline"?

The baseline will be allowed to vary by no more that 4 points on a 10 point scale for any patient which is enrolled in the study. Any patient who varies by more than 4 points would not be allowed in the study. The division concurs

- When will the patients be randomized?

The patients will be randomized before baseline measurements. The division is concerned with post randomization exit if the patient does not meet the baseline definition criteria. The division recommends randomizing post baseline meansurements. The sponsor will consider this recommendation.

- How many patients will be in the study?

There will be approximately 40 patients in the study.

- What is the definition of "exit" from treatment.

If the patient experiences 48 hours or increased pain, 4 points on the VAS scale, or decreased pain, 2 points on the VAS scale, and wants to exit the study, the patient will leave the treatment he is on and go tho the open label portion of the study. The division concurs.

If the patient does not acheived either increased or decreased pain levels as specified above, he will not be counted as a failure and will get a VAS score upon dropout. The sponsor is encouraged to follow the patient on a daily basis.

- The division recommends that an assessment of blinding be conducted at 48 hrs.

The sponsor will consider doing an assessment of blinding at 48 hrs by asking the patient " what were you on and why do your think so?" The sponsor will incorporate this in the final revised protocol.

- Will a 2 tail test or a 1 tail test be conducted for efficacy (page 10)?

The sponsor will clarify whether a one or two tail test will be used for final analysis. The division recommends a two tail test for the basis of Approval.

- What is the sponsor's intent for "drop outs? What is the meaning of "high level"?

The sponsor will submit a response to clarify the meaning of "high level" of drop outs.

- The division is willing to review and provide comments on a revised protocol based on today's telecon.

The sponsor has proposed a cross over design study. It would be basically the study already proposed but with an add-on component of the patients being treated by the "other test drug" at the end of the study. The division reserves comments until a revised protocol is submitted. The sponsor is asked to declare a primary analysis for the basis of review.

FOLLOW UP:
The sponsor sent in a protocol dated October 18, 1997.
We had a telecon with the sponsor on November 18, 1997.
The Division has no objections at this time to the proposed a cross-over design protocol. The Division, however, does require the sponsor to declare a primary analysis prior the start of the study.

ACTION:
The sponsor will send in a revised protocol which declares a primary analysis.

Submitted by Chin Koerner ____/S/____ 11/23/97 Project Manager
saved as tc7.017

cc:
NDA 20-612
Div Files
HFD-550/ Koerner